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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
TON, THAIAN N	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 11/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/881,204	DOMINKO ET AL.	
	Examiner	Art Unit	
	Thaian N. Ton	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 8/23/04.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 48-98 and 101-127 is/are pending in the application.

4a) Of the above claim(s) 69,86-97,101-119 and 125 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 48-68,70-85,98,120-124,126 and 127 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants' Amendment, filed 8/23/04, has been entered. Claims 48, 98, 101, 105, 116, 118, 119, 122, 123, 124, 127 have been amended. Claims 48-98, 101-127 are pending. Claims 69, 86-97, 101-119 and 125 are withdrawn. Claims 48-68, 70-85, 98, 120-124, 126 and 127 are under current examination.

Claim Amendments

Claim 69 has been given an inappropriate claim identifier. The identifier states 'previously presented'. The appropriate identifier for this claim should be: withdrawn. Appropriate correction is required.

Claim Rejections - 35 USC § 101

The prior rejection of claims 99 and 100 under 35 U.S.C. 101 is rendered moot in view of the cancellation of the claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The prior rejection of claims 48-68, 70-85, 98 120-124, 126 and 127 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement

is maintained for reasons of record. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims, as currently amended, are directed to methods of generating a hybrid mammalian cell by preparing more than one cytoplast fragment from a mammalian oocyte or fertilized zygote; obtaining a nuclear donor cell or karyoplast taken from the mammal, combining a cytoplast fragment with a nuclear donor cell or karyoplast to produce a hybrid mammalian cell; and if an oocyte is used, then activating the oocyte before, during, or after combining the cytoplast with the nuclear donor cell.

Applicants argue that the recitation of "hybrid" cells in the claims obviates the prior enablement rejection. See p. 14 of the Response. This is not persuasive. The claims as amended are not enabling because the specification fails to provide any other enabled use for the hybrid mammalian cells, other than as pluripotent cells. See p. 8, ¶ 0018, which states, "The invention is of the production of pluripotent cells using cytoplast fragments obtained from either whole enucleated oocytes or whole, enucleated fertilized zygotes." The specification teaches that the resulting hybrid cell is maintained in an undifferentiated state and then can be induced to differentiate into a desired cell type, and can ultimately be used for transplantation. See also, p. 12, ¶ 0037-0038. Thus, as stated in the prior Office

action, the specification fails to provide sufficient teachings with regard to the generation of the hybrid mammalian cells, such that they would be considered pluripotent.

The instant specification does not contemplate any other use of the hybrid mammalian cells, other than in the context of pluripotent cells. Thus, it is reiterated the instant specification fails to provide teachings or guidance to show that the resulting hybrid cells are, indeed, pluripotent. The specification defines *pluripotent* as, "A cell that is capable, through its progeny, of giving rise to all cell types which comprise the adult animal including the germ cells." See p. 14, ¶ [0049]. The working examples provided by the specification fail to show pluripotency in the resulting hybrid cells. Example 3, which describes the production of porcine-bovine hybrid cells, states that cell colonies that appeared in culture "aggregated into an embryoid body or mass" and then speculates that these cells have a potential to differentiate. The cells of Example 3 were then described to have a different morphologies, which "resemble " embryonic stem cells. Further, Example 5 teaches the generation of myocardial-like cells, which were observed to be beating. The specification fails to teach specific characterization of the hybrid cells such that one of skill in the art would be able to identify them as *pluripotent.* Thomson, cited in the prior Office action, teaches the specific, art-recognized characteristics of pluripotent cells – that these cells remain undifferentiated in culture in continuous passage, maintain a normal karyotype, express appropriate

cell markers [alkaline phosphatase, SSEA-3, SSEA-4, TRA-160-, TRA-1-81] and, when injected into SCID mice, they consistently differentiate into derivatives of all three germ layers. See *Abstract* and p. 7845-7846. It is reiterated that the instant specification fails to provide characterization of the claimed cells, other than description of a morphology that resembles ES cells, and the generation of myocardial-like cells, which were observed to beat. This is not sufficient to demonstrate that the claimed cells are capable of, for example, give rise to all cell types, as required by both the instant specification's definition of pluripotent, and the art-recognized definition of the term. The specification fails to teach analysis of the hybrid cells to show that they exhibit these art-recognized characteristics of pluripotent cells.

Applicants argue, that with regard to the mammalian oocyte that would be used in the claimed methods, that the art teaches that other types of oocytes can be used in NT methods. Applicants point to Miyoshi et al. which teaches metaphase I oocytes, and Baguisi who teach the use of telophase II oocytes. See p. 14, 4th ¶ of the Response. Neither of these references has been provided by Applicants, thus, they have not been considered. However, it is noted that the prior Office action explicitly states that the oocytes which are known by the art to be used in successful NT methodology are MII oocytes and oocytes in telophase II (see p. 7-8 of the prior Office action). This supports the Baguisi reference, which Applicants have cited.

Applicants further argue 1) oocytes may be discovered in the future and 2) the type of oocytes are not relevant, because any oocyte that can be used for NT, which is known to those skilled in the art of cloning, could be used. See p. 15, 1st ¶ of the Response. This is not persuasive, because the specification must be enabled at the time of filing. See MPEP § 2164.05 (a), which states:

> The state of the prior art provides evidence for the degree of predictability in the art and is related to the amount of direction or guidance needed in the specification as filed to meet the enablement requirement. The state of the prior art is also related to the need for working examples in the specification. The state of the art for a given technology is not static in time.

Thus, the state of the prior art provides evidence that particular types of oocytes would be considered enabled for the claimed NT methods. Furthermore, the claims recite the generation of hybrid mammalian cells, wherein the specification teaches their enabled use as pluripotent cells. In order to produce the hybrid cells, the specific nuclear transfer method steps must be enabled. Thus, as the state of the art clearly provides evidence that only MII and telophase oocytes were considered routine and predictable in nuclear transfer methods. Thus, it is maintained that the type of oocyte that would be used in the instantly claimed methods is relevant to the enablement of those methods.

Applicants' amendments to the claims now with the recitation of an activation step of the NT unit, is found to be persuasive. Applicants' arguments, with regard to the instantly claimed methods drawn to producing hybrid

mammalian cells, and not cloning animals, is found to be persuasive. See p. 15 of the Response.

Accordingly, the Examiner has clearly provided evidence for the unpredictability of the NT art, as such specific guidance must be provided by the specification. However, the instant specification fails to provide teachings or guidance to overcome these unpredictabilities. One of skill in the art could not rely on the state of the art, because it is replete with teachings to show NT's unpredictability for any donor cell and any recipient oocyte, as broadly claimed. Accordingly, in view of the undeveloped and unpredictable state of the art with regard to NT, it would have required undue experimentation for one of skill in the art to carry out the claimed methods.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The prior rejections of claims 99 and 100 as being anticipated by WO 97/07668, Campbell *et al.*, Wolf *et al.*, Susko-Parrish *et al.*, Sims *et al.*, Robl *et al.* is rendered moot in view of Applicants' cancellation of the claims.

The prior rejection of claims 47-57, 60-64, 66, 67, 70-74, 77, 78, 81, 82, 98, 123, 124, and 127 is *maintained* under 35 U.S.C. 102(b) as being anticipated by Peura [cited in the prior Office action] is for reasons of record.

Applicants argue that the instant claims inherently require a decrease in the total amount of cytoplasm contributed by the cytoplast, and that because claims are read in light of the teachings of the specification, and the specification clearly teaches that the enucleated cytoplast fragments are fractions of an oocyte, which constitute less than the entire cytoplasm, and that "smaller volume of cytoplasts will produce fewer problems of mitochondrial incompatibility." See p. 16, 2nd ¶ of the Response.

This is not found to be persuasive. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., a decrease in the total amount of cytoplasm contributed by the cytoplast) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The claims are directed to preparing more than one cytoplast fragment for use in nuclear transfer methodology. There is no size or functional limitation to the cytoplast fragment. The specification simply teaches that a cytoplast fragment is enclosed by a membrane and is a fragment of an oocyte or fertilized zygote which is less than the entire cytoplasm of the oocyte and lacks a

nucleus or nuclear DNA material. See ¶ 0041. The specification provides no discussion with regard to the decrease in cytoplasm will produce fewer problems of mitochondrial incompatibility. Thus, Peura fulfills these limitations and for reasons of record advanced in the prior Office action.

Accordingly, it is maintained that Pleura anticipate the claimed invention.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Thaian N. Ton whose telephone number is (571) 272-0736. The Examiner can normally be reached on Monday through Friday from 8:00 to 5:00 (Eastern Standard Time), with alternating Fridays off. Should the Examiner be unavailable, inquiries should be directed to Amy Nelson, Acting SPE of Art Unit 1632, at (571) 272-0804. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 872-9306.

tnt
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